

### **Listing of Claims**

1. (Original) A method of proposing new genomic/proteomic-related knowledge, the method comprising the steps of:
  - a) providing a representation structure for genomic/proteomic-related concepts comprising
    - i) nodes representative of known genomic/proteomic information selected from the group consisting of, conditions, processes, and physical structures, and
    - ii) qualitative descriptors representative of interrelationships among nodes;
  - b) proposing a biological model using said representation structure and specifying plural pairs of nodes and descriptors between selected nodes from said representation structure;
  - c) simulating the proposed biological model to produce simulated data;
  - d) assigning a fitness measure to the proposed biological model as a measure of how the simulated data compares to said data representative of measured biological behavior or properties;
  - e) repeating steps b) through d) for a plurality of different proposed biological models; and
  - f) selecting one of said different proposed biological models in response to the fitness measures of said plurality of biological models.
2. (Original) The method of claim 1, wherein said biological model is proposed using an evolutionary algorithm.
3. (Original) The method of claim 1, wherein said biological model is proposed using genetic programming or a genetic algorithm.

4. (Original) The method of claim 1, wherein said biological model comprises a population of biological models.
5. (Original) The method of claim 1, wherein said method comprises an additional step of proposing new biological models using models simulated and scored in step d) by applying genetic algorithm crossover techniques.
6. (Original) The method of claim 5, wherein said genetic algorithm crossover techniques comprise mutation or probabilistic selection.
7. (Original) The method of claim 1, wherein said proposed biological model includes nodes of established position interconnected by established descriptors.
8. (Original) The method of claim 1, wherein said representation structure further comprises differential equations quantitatively representing possible relationship between pairs of nodes.
9. (Original) The method of claim 1, wherein qualitative simulation techniques are used to simulate the proposed model to produce simulated data.
10. (Original) The method of claim 1, comprising repeating said method using datasets probing disparate biological subsystems or substructures and combining models of said disparate subsystems or substructures into a consolidated model.

11. (Original) The method of claim 1, comprising repeating said method using datasets probing networks within a physiological pathway, cell compartment, cell, organism, population, or ecological system to discover subsystem networks, and combining disparate subsystem networks into a consolidated network.
12. (Original) The method of claim 1, wherein said nodes comprise enzymes, cofactors, enzyme substrates, enzyme inhibitors, DNAs, RNAs, transcription regulators, DNA activators, DNA repressors, signaling molecules, trans membrane molecules, transport molecules, sequestering molecules, regulatory molecules, hormones, cytokines, chemokines, antibodies, structural molecules, metabolites, vitamins, toxins, nutrients, minerals, agonists, antagonists, ligands, receptors, or combinations thereof.
13. (Original) The method of claim 1, wherein said nodes comprise protons, gas molecules, small organic molecules, amino acids, peptides, protein domains, proteins, glycoproteins, nucleotides, oligonucleotides, polysaccharides, lipids, glycolipids, or combinations thereof.
14. (Original) The method of claim 1, wherein said nodes comprise protein complexes, protein-nucleotide complexes, cell compartments, organelles, membranes, or combinations thereof.
15. (Original) The method of claim 1 wherein said nodes comprise descriptors or networks of nodes and descriptors comprising a substructure or sub-network of a biological system.
16. (Original) The method of claim 1, wherein said nodes comprise cells, tissues, or organs.

17. (Original) The method of claim 1, wherein said nodes comprise drug candidate molecules.
18. (Original) The method of claim 1, wherein said nodes are individuals of a species.
19. (Original) The method of claim 1, wherein said data representative of measured biological behavior or properties comprises data representative of experimental data, knowledge from the literature, patient data, clinical trial data, compliance data; chemical data, medical data, or hypothesized data.
20. (Original) The method of claim 1, wherein said data representative of measured biological behavior or properties comprises data acquired using PCR, qualitative PCR, gene expression assays, or protein arrays.
21. (Original) The method of claim 1, comprising the additional step of conducting biological experiments designed to assess the validity of a proposed biological model.
22. (Original) A method of proposing new life-sciences related knowledge, the method comprising the steps of:
  - a) providing a case frame structure for life-science related concepts comprising
    - i) nodes representative of known life-sciences information selected from the group consisting of, conditions, processes, and physical structures, and
    - ii) case frames representative of interrelationships among nodes;
  - b) proposing a biological model using said case frame structure and specifying plural pairs of nodes and descriptors between selected nodes from said case frame structure;
  - c) simulating the proposed biological model to produce simulated data;

d) assigning a fitness measure to the proposed biological model as a measure of how the simulated data compares to said data representative of measured biological behavior or properties;

e) repeating steps b) through d) for a plurality of different proposed biological models; and

f) selecting one of said different proposed biological models in response to the fitness measures of said plurality of biological models.

23. (Original) The method of claim 22, wherein said biological model is proposed using an evolutionary algorithm.

24. (Original) The method of claim 22, wherein said biological model is proposed using genetic programming or a genetic algorithm.

25. (Original) The method of claim 22, wherein said biological model comprises a population of biological models.

26. (Original) The method of claim 22, wherein said method comprises an additional step of proposing new biological models using models simulated and scored in step d) by applying genetic algorithm crossover techniques.

27. (Original) The method of claim 26, wherein said genetic algorithm crossover techniques comprise mutation or probabilistic selection.

28. (Original) The method of claim 22, wherein said proposed biological model includes nodes of established position interconnected by established descriptors.

29. (Original) The method of claim 22, wherein said representation structure further comprises differential equations quantitatively representing possible relationship between pairs of nodes.

30. (Original) The method of claim 22, wherein qualitative simulation techniques are used to simulate the proposed model to produce simulated data.

31. (Original) The method of claim 22, comprising repeating said method using datasets probing disparate biological subsystems or substructures and combining models of said disparate subsystems or substructures into a consolidated model.

32. (Original) The method of claim 22, comprising repeating said method using datasets probing networks within a physiological pathway, cell compartment, cell, organism, population, or ecological system to discover subsystem networks, and combining disparate subsystem networks into a consolidated network.

33. (Original) The method of claim 22, wherein said nodes comprise enzymes, cofactors, enzyme substrates, enzyme inhibitors, DNAs, RNAs, transcription regulators, DNA activators, DNA repressors, signaling molecules, trans membrane molecules, transport molecules, sequestering molecules, regulatory molecules, hormones, cytokines, chemokines, antibodies, structural molecules, metabolites, vitamins, toxins, nutrients, minerals, agonists, antagonists, ligands, receptors, or combinations thereof.

34. (Original) The method of claim 22, wherein said nodes comprise protons, gas molecules, small organic molecules, amino acids, peptides, protein domains, proteins, glycoproteins, nucleotides, oligonucleotides, polysaccharides, lipids, glycolipids, or combinations thereof.
35. (Original) The method of claim 22, wherein said nodes comprise protein complexes, protein-nucleotide complexes, cell compartments, organelles, membranes, or combinations thereof.
36. (Original) The method of claim 22, wherein said nodes comprise descriptors or networks of nodes and descriptors comprising a substructure or sub-network of a biological system.
37. (Original) The method of claim 22, wherein said nodes comprise cells, tissues, or organs.
38. (Original) The method of claim 22, wherein said nodes comprise drug candidate molecules.
39. (Original) The method of claim 22, wherein said nodes are individuals of a species.
40. (Original) The method of claim 22, wherein said data representative of measured biological behavior or properties comprises data representative of experimental data, knowledge from the literature, patient data, clinical trial data, compliance data; chemical data, medical data, or hypothesized data.

41. (Original) The method of claim 22, wherein said data representative of measured biological behavior or properties comprises data acquired using PCR, qualitative PCR, gene expression assays, or protein arrays.

42. (Original) The method of claim 22, comprising the additional step of conducting biological experiments designed to assess the validity of a proposed biological model.